(i) an effective amount of at least one supplement selected from the group consisting of a growth factor, an antibody, a polynucleotide or oligonucleotide, a cytotoxin or cell proliferation inhibiting compound, an osteogenic or cartilage inducing compound, an antimicrobial composition, an analgesic, an anesthetic, an anticoagulant, an antiinflammatory compound, a cytokine, a chemotherapeutic drug, a hormone, an interferon, a lipid, a polysaccharide, a protease inhibitor, a proteoglycan, a steroid, a vasoconstrictor, a vasodilator, a vitamin, and a nutritional mineral, and

Mr.

(ii) a biocompatible tissue sealant composition comprising fibrinogen or a derivative or metabolite thereof in an amount which [is capable of forming] forms a fibrin matrix [in the presence of thrombin, Factor XIII and Ca⁺⁺].

E Joseph S

- 13. (Amended) The delivery system of claim 12, wherein [the supplemented tissue sealant composition] said delivery system is [delivered] placed in close proximity to tissue of a patient, thereby permitting the localized release of said [antibody] supplement to the tissue of said patient.
- 14. (Amended) The delivery system of [claims 12 or] <u>claim</u> 13, wherein said localized release of [the antibody] <u>said supplement</u> is sustained release.
- 15. (Amended) The delivery system of claims claim 14, wherein [the antibody] said supplement is of sufficiently low solubility to permit localized, sustained-release of [antibody] said supplement.

BEST AVAILABLE COPY

- 16. (Amended) The delivery system of [claims] claim 14, wherein the mass of [antibody] supplement exceeds an amount which is soluble in [the volume of] the fibrin matrix, thereby permitting localized, sustained-release of [antibody] said supplement.
- 17. (Amended) The delivery system of claim [16] 14, wherein said [antibody] supplement is introduced into said [matrix] biocompatible tissue sealant composition as an emulsion.
- 18. (Amended) The delivery system of [claims] <u>claim</u> 14, wherein said [antibody] <u>supplement</u> interacts with said fibrin matrix, thereby permitting localized, sustained-release of said [antibody] <u>supplement</u>.
- 19. (Amended) The delivery system of claim 14, wherein said [antibody] supplement is in solid form.
- 20. (Amended) The delivery system of claim 19, wherein said [antibody] <u>supplement</u> is introduced into said [matrix] <u>biocompatible tissue sealant composition</u> in solution in a carrier, said carrier having a higher rate of dissolution <u>or diffusion in said fibrin matrix</u> than said composition contained therein, so that [the composition] <u>said supplement</u> is deposited within [the] <u>said fibrin</u> matrix as a solid precipitate.

Please add the following new claims 24-33:

BEST AVAILABLE COPY

Jub 2

The delivery system of claim 13, wherein said supplement is a cytotoxin or cell proliferation inhibiting compound and said tissue is a neoplastic or hyperproliferative lesion of a patient and tissue adjacent thereto.

25. The delivery system of claim 12, wherein said supplement is a growth factor selected from the group consisting of: fibroblast growth factors; platelet-derived growth factors; insulin-binding growth factors; epidermal growth factors; transforming growth factors; cartilage-inducing factors; osteoid-inducing factors; osteogenin and other bone growth factors; bone morphogenetic growth factors; collagen growth factors; heparin-binding growth factors; cytokines; interferons; hormones and biologically active derivatives of said growth factors.

- 26. The delivery system of claim 12, wherein said supplement is an osteogenic or cartilage inducing compound selected from the group consisting of: cartilage-inducing factors; osteoid-inducing factors; osteogenin and other bone growth factors which modulate the proliferation, migration and/or attraction of progenitor bone cells; bone morphogenetic growth factors; demineralized bone matrix; and biologically active derivatives of said compounds.
 - 27. The delivery system of claim 12, wherein said supplement is an antibody.
- 28. The delivery system of claim 12, wherein said supplement is a polynucleotide or an oligonucleotide.

N

Mb (3

John

BEST AVAILABLE COP'

- 29. The delivery system of claim 12, wherein said supplement is an antimicrobial compound.
- 30. The delivery system of claim 12, wherein said biocompatible tissue sealant composition further comprises thrombin or other activator of fibrin formation.
- 31. The delivery system of claim 12, wherein said biocompatible tissue sealant composition further comprises Factor XIN.
- 32. The delivery system of claim \(\)2, wherein said biocompatible tissue sealant composition further comprises Ca⁺⁺.
- 33. The delivery system of claim 14, wherein said supplement is introduced into said biocompatible tissue sealant composition in solution in a carrier, \-

Remarks

In view of the foregoing amendments and the following remarks, Applicants respectfully request reconsideration and withdrawal of all outstanding objections and rejections and early allowance of the above-identified application.

Upon entry of the foregoing amendment, claims 12-33 are pending in the application, with claim 12 being the sole independent claim. New claims 24-33 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

BEST AVAILABLE COP

10 Pro Court